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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,975	04/07/2004	Daniel Santi	020547-003700US	9532

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/820,975	SANTI ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/28/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *21-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' election without traverse of the invention of Group I, drawn to a method of ligation of a plurality of DNA segments, in the reply filed on 02/28/2006 is acknowledged. The species election requirement is withdrawn since it did not require separate searches in the patent and non-patent literature.

Claims 21-30 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim.

Claims 1-20 are pending.

Double Patenting

2. Applicant is advised that should claim 8 be found allowable, claim 9 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Siegal et al. (BioTechniques, 1996, 21, p. 614 and 617-619).

Siegal et al. teach a ligation reaction containing three DNA fragments (p. 614, third column). Siegal et al. teach obtaining the fragments by cleaving the DNA molecules to generate segments with two ligatable ends, each ligatable end having a region of identity with an adjacent segment, wherein at least one segment comprises two libatable ends; simultaneous ligation of the three segments results in a DNA molecule having the fragments assembled in a predetermined order (p. 617, column 2, p. 618, Fig. 1). Siegal et al. also teach selection of the ligation product with the desired, predetermined order (p. 618, column 2). Since Siegal et al. teach all the limitation of the instant claim, the claimed invention is anticipated by the above-cited art.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Mandecki et al. (Gene, 1988, 68: 101-107).

Mandecki et al. teach synthetic generation of genes by directional assembling in a single ligation reaction of eight DNA fragments. Mandecki et al. teach cleaving of the DNA molecules comprising the gene segments to produce DNA segments with ligatable ends, each ligatable end comprising a region having sequence identity with an adjacent

DNA segment, wherein at least one segment comprises two ligatable ends, and simultaneously ligating each segment to the adjacent segment in the predetermined order to create the gene (p. 102, column 2, second paragraph, p. 103, column 3, second paragraph). Mandecki et al. also teach selecting for the product of the ligation reaction (p. 103, column 2, last paragraph). Since Mandecki et al. teach all the limitation of the instant claim, the claimed invention is anticipated by the above-cited art.

5. Claims 1-6 and 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Santi et al. (PGPUB 2004/0166567).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Santi et al. teach a method of synthesis of genes encoding large polypeptides, such as polyketide synthase (PKS) (p. 9, paragraph 0105). Santi et al. teach a method of joining a series of at least three or more DNA units to generate a DNA construct by combining at least three synthons. The synthons are provided in vectors (type I, II, and III DNAs) that each contains a first selectable marker that is different in each vector and, optionally, a second selectable marker; each synthon is flanked by two restriction sites recognized by a first Type IIS restriction enzyme and a second Type II restriction

enzyme (p. 2, paragraph 0019, p. 15, paragraph 0156, p. 16, paragraph 0197). The vectors are digested with the respective restriction enzymes to generate vector fragments with compatible (cohesive, i.e., single-strand overhang) ends outside the synthon sequences that can be ligated to generate a new selectable vector containing the joined synthon sequences in a predetermined order (p. 12, paragraph 0155). Santi et al. teach that the counter-selectable marker could be *ara*B and the first and second selectable markers are genes that confer drug resistance (p. 16, paragraph 0212). Santi et al. also teach transforming cells with the ligation product and selecting transformants the first and second selectable markers and isolating the ligation product comprising the ligated synthons in a predetermined order (p. 13, paragraph 0159, p. 16, paragraphs 0201 and 0207). Since Santi et al. teach all the limitation of the instant claims, the claimed invention is anticipated by the above-cited art.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebedenko et al. (Nucleic Acids Research, 1991, 19: 6757-6761), in view of Gokhale et al. (Science, 1999, 284: 482485), as evidenced by Slater et al. (PGPUB 2005/0074883).

Lebedenko et al. teach a method of ligation of a plurality of DNA segments to obtain a ligation product that contains sequences from each DNA segment in a predetermined order (Abstract). Lebedenko et al. teach synthesizing the IL-1α gene by providing three DNA molecules, each having a first and a second cleavage site recognized by type IIS restriction endonucleases, cleaving each DNA molecule with the appropriate restriction endonucleases, simultaneously ligating the resulting cleaved segments, and isolating the ligation product (p. 6757, column 2, p. 6758, columns 1 and 2). With respect to the limitation of the DNA molecules each having a selectable marker and a counter-selectable marker, this is not innovative, the prior art teaches the use of diverse selectable and counter-selectable markers and combinations thereof (see Slater et al.). One of skill in the art would know to use the right combination of selectable and counter-selectable markers for the selection of the desired product. Lebedenko et al. do not teach PKS. Gokhale et al. teach recombining modules from the naturally-occuring PKSs (p. 482, column 2). With respect to the limitation of the presence of at least two Type 3 DNA molecules, one of skill in the art would know to use more than one molecule, depending on the gene nedded to be synthesized. It would have been obvious to one of skill in the art, to use the method of Lebedenko et al. to obtain synthetic PKSs as taught by Gokhale et al., with a reasonable expectation of success. The motivation to do so is provided by Gokhale et al. who teach PKSs have a modular structure, and novel combinations of modules could result the synthesis of diverse medicinally important new product (Abstract, p. 482, column 1). One of skill in the art would have been expected to have a reasonable expectation of success in making such

synthetic genes because Lebedenko et al. teach the successful *in vitro* synthesis of genes by their method. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

8. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford
Primary Examiner
AU 1633

Ileana Popa